zone in late reperfused myocardial infarction (3), which is unlikely to be related to actual salvage but more likely reflects an inflammatory response of adjacent tissue, is possibly related to reperfusion injury. Moreover, in several studies, the area at risk was consistently larger in the group with more severe injury as indicated by myocardial hemorrhage (5).

Because the histologic assessment of myocardial edema is challenging and virtually impossible in clinical models, experimental and clinical research will have to use CMR and careful study designs to scrutinize the impact of reperfusion and other, less important potential confounders on the extent of myocardial edema.

Despite these knowledge gaps, there is solid evidence that T2-weighted imaging is closely correlated with the area at risk in reperfused MI and, in combination with late Gd enhancement imaging, allows for the assessment of myocardial salvage. Before having a more clear understanding of confounders, it may be too early to claim a precision in the <10% range. Clearly, further studies are required to understand the impact of potential clinical confounders, yet there is little doubt that the available techniques provide unique invaluable in vivo data on myocardial injury in patients with reperfused MI.

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## REPLY

We thank Dr. Mewton and colleagues for adding to the discussion regarding T2-weighted cardiac magnetic resonance (CMR). Often, a candid debate will invoke strong reactions, but we are hopeful that readers of our Pro/Con article (1) with Dr. Friedrich will carefully consider the merits of the respective arguments. Here, we present our perspective on the issues raised by Dr. Mewton and colleagues.

At the outset, philosophically, we take exception to the comment that: "*As always, in such a debate truth probably relies somewhere in between.*" At issue is whether or not T2-weighted CMR depicts post-infarct myocardium at risk. Fundamentally, it can only be one or the other.

With regard to the other issues raised:

1. We agree that T2-CMR can show myocardial edema—which we believe is a marker of necrosis in the setting of acute ischemic injury.

2. We agree that T2-CMR can provide incremental data to delayed-enhancement imaging.

3. We agree that T2-short tau inversion recovery (as well as double-inversion T2-turbospin echo) is sensitive to many artifacts. These artifacts may be indistinguishable from true abnormalities and/or render images non diagnostic. As such, we believe that "classic," black-blood T2-CMR is often neither convenient nor simple.

4. We strongly disagree that myocardial edema correlates with the myocardial area at risk (AAR). As we note in our paper, (1) the fundamental problem is that the underlying physiology is incompatible with this hypothesis. With respect to water content (and many other physiological parameters), it is well-known that the post-infarct AAR is markedly heterogeneous, with the infarcted portion having 10-fold or more edema than the salvaged, viable portion. While newer pulse sequences may improve image quality, these methods will not overcome this fundamental issue.

5. We agree that from a pathophysiological perspective, assuming that there is a direct linear relationship between the AAR (simply the perfusion territory of an epicardial coronary artery) and myocardial edema is highly problematic. T2-CMR does not index perfusion, but instead reflects dynamic and complex changes occurring within infarcted myocardium, including inflammation, hemorrhage, and microvascular obstruction, among others.

6. We are puzzled regarding the comment on interstitial edema. Because the literature is quite clear that total water content is not appreciably elevated within salvaged myocardium, it is unclear how interstitial or any other form of edema can provide a mechanism for the depiction of the AAR.

7. We disagree that delayed-enhancement CMR overestimates infarct size in the acute setting. A definitive validation study (2) should take precedence over reports—even if several—in which the "evidence" is simply size differences measured on CMR datasets, often with variable image quality.

8. Finally, with regard to the possibility that the combination of "early" and conventional "late" gadolinium-enhanced CMR can depict salvaged myocardium (3), we are disheartened by the line of reasoning that afflicts this and the majority of T2-CMR reports—namely that size differences between 2 CMR depictions of the "abnormal" zone must represent a pathophysiology. Presumably, most practitioners would not assume that the consistent overestimation of left ventricular mass as measured by gradient-echo cine-CMR as compared with steady-state free precession cine-CMR reflects a new pathophysiology.

The physiological basis for interpreting "early" delayed enhancement or T2-CMR hyperintensity as the area-at-risk is poorly described and/or inconsistent with known precepts. We are left to conclude that with new imaging techniques, it is paramount that definitive pathology-based validation studies be performed. If appropriate vali-

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dation data is absent, the focus should be on how the underlying physiology informs cardiac imaging and not the other way around.

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